Rearrangements in Asymmetric Synthesis of Drug and Natural Product Scaffolds

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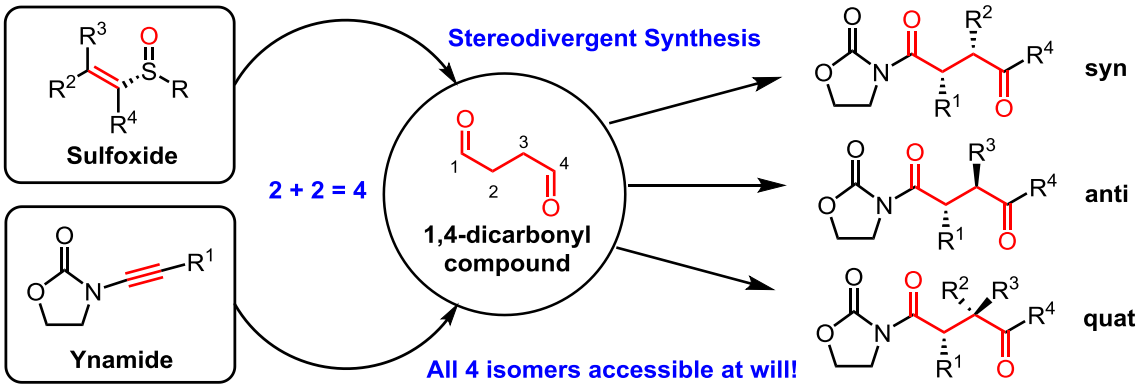
The chemistry of carbonyl group is essential to modern organic synthesis. The preparation of 1,3- or 1,5-dicarbonyls is well developed, as this disconnection naturally follows from the intrinsic polarity of the carbonyl groups. By contrast, a general enantioselective access to quaternary stereocenters in acyclic 1,4-dicarbonyl systems remains an unresolved problem, despite the tremendous importance of 2,3-substituted 1,4-dicarbonyl motifs in natural products and drug scaffolds.



Here we present broad enantioselective and stereodivergent strategy to access acyclic polysubstituted 1,4-dicarbonyls *via* acid-catalyzed [3,3]-sulfonium rearrangement starting from alkenyl sulfoxides and ynamides. The stereochemistry at sulfur governs the absolute sense of chiral induction, whereas the double bond geometry dictates the relative configuration of the final products.[1] Moreover, we have also demonstrated, that enantioenriched aryl sulfoxides and ynamides similarly afford chiral α-arylated amides and thioesters in an atom-economical manner.[2,3]

[1] D. Kaldre, I. Klose, N. Maulide, *Science*, **2018**, *361*, 664-667.
[2] D. Kaldre, B. Maryasin, D. Kaiser, L. Gonsalez, N. Maulide, *Angew. Chem. Int. Ed.*, **2017**, *56*, 2212-2215.
[3] B. Maryasin, D. Kaldre, *et. al.*, *Chem. Sci.*, **2018**, *9*, 4124-4131.